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A3243G Mitochondrial DNA Mutation does not Play an Important Role among DM Population in Indonesia

Abstract

Diabetes mellitus (DM) is a polygenic complex disorder, characterized by a disturbance in insulin production by the pancreatic beta-cell or in the ability of target tissues to respond to insulin. The adult onset non-insulin dependent or type 2 DM, in particular, clearly demonstrates the interplay between genetic and nutritional factors in the pathomechanism of this disorder. The importance of the mitochondrial genetic factors in its pathogenesis has long been suggested, and several mutations in the mitochondrial DNA (mtDNA) are indeed expressed as DM. Of more than 70 mtDNA mutations that have been suggested to be associated with DM, only one, an A3243G substitution in the tRNAleu gene, is in fact firmly established to be causal for DM. The finding of the mtDNA A3243G mutation as an important causal mutation for MDM has been confirmed for a variety of racial backgrounds. For the Caucasians, the contribution of A3243G mutation has been investigated in the Netherlands, France, United Kingdom, Germany and Japan; the prevalence of MDM seems to be similar in those countries, about 1.5 %, and 2-5 times higher in cases with family history. In the Chinese, the mutation was detected in about 2.5% unrelated patients with T1DM and T2DM. In this present study, the aim was to seek A3243G mtDNA mutation related to DM. Blood DNA was screened from 451 of T2DM cases collected from DM patients at Dr. Soetomo Hospital during 2001-2003. The A3243G was detected using the Polymerase chain reaction (PCR) and digested with Apal restriction enzyme. DNA sequencing was planned to confirm if the mutation will be found. The results indicated the absence of A3243G mutation in the study population. Thus, other genetic factors, which could be of the nuclear or mitochondrial genomes, appeared to modulate the expression of the A3243G mutation allowing its clinical detection as MELAS or DM, or to increase the recurrent occurrence of the mutation. Such a scenario has been suggested for the G11778C mutation in the mtDNA that underlies Leber’s Hereditary Optic Neuropathy (LHON). This recurrent mtDNA mutation has been shown to be associated with mtDNA haplogroup J in Europeans, and haplogroups M and BM in Southeast Asians.

Keyword : mitochondrial, DNA, mutation, monogenic, polygenic, diabetes, mellitus, maternally, inherited, single, nucleotide, polymorphism, A3243G,